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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/753,313	12/29/2000	Gerardo Castillo	PROTEO.P16	1184

7590 06/09/2005

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EXAMINER	
TATE, CHRISTOPHER ROBIN	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/753,313	CASTILLO ET AL.	
	Examiner	Art Unit	
	Christopher R. Tate	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,5,10 and 28-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *4,5,10 and 28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *1104*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 01 April 2005 is acknowledged and has been entered. Claims 4, 5, 10, and 28-32 have been examined on the merits. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4, 5, 10, and 28-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The newly recited claim limitations "such that it is the therapeutic amount of the substance administered that treats or disrupts the amyloid fibrils" (claims 4, 28, and 31) and "produced by process have the steps of (1) water extraction, using water this is not boiling" (claim 31) are deemed new matter as no literal support for these limitations were found in the instant disclosure. Although Applicants state that no new matter was added by these claim amendments and that instant Example 1 set forth the process of water extraction using water that is not boiling, no support could be found therein (including the exclusion of boiling water). It is requested that Applicants particularly point to support for the cited phrase limitations above within the instant specification or, alternatively, to omit these recitations from the claims.

Claim Rejections - 35 USC § 102

Claims 4, 5, and 28-31 stand/are rejected under 35 U.S.C. 102(b) as being anticipated by Mitsui Norin (JP 10-245342), or by Takami et al. (JP 10-175858) for the reasons set forth in the previous Office action which are restated below.

Mitsui Norin teaches the administration (e.g., in oral dosage form) of a therapeutically effective amount of epicatechin (which is a naturally occurring compound extracted from green tea) as well as green tea extract, to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to the deposition of beta-amyloid protein on brain nerve cells and, thus, reduce the toxicity of beta-amyloid protein (which is medically well known to be responsible for amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence). See entire English translation of this JP patent.

Takami et al. teach the administration (e.g., in the form of a pharmaceutical tablet, capsule, etc; or within a consumable drink or food, etc) of a pharmacologically effective amount of a green tea extract (termed TEAFURAN 30) containing epicatechin therein, or a component thereof - such as epicatechin, including to someone suffering from Alzheimer's disease brought about by toxicity of beta amyloid protein (see discussion above with respect to such toxicity). See entire computer-generated English translation of the JP patent. Please note that such an amount would inherently be in an amount to provide the functional effect(s) instantly claimed.

As set forth in previous Office action, the above reference methods would inherently provide the functional effects instant claimed - i.e., would inherently treat, inhibit, or manage amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence in a subject suffering from Alzheimer's disease upon such oral consumption.

Therefore, each of the cited references is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

Claims 4, 5, 10, and 28-32 stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitsui Norin and Takami et al. (JP 10-175858), in view of Chatterjee et al. (US 4,892,883) as well as the recognized state of the art for the reasons set forth in the previous Office action which are restated below.

The primary references are relied upon for the reasons discussed *supra*. Neither of these references expressly teach the further inclusion of the herbal agents instantly recited in claim 10.

Chatterjee et al. beneficially disclose that administration of *Ginkgo biloba* is useful in the therapy of Alzheimer's disease (see, e.g., col 7, lines 13-39). In addition, it is noted that none of the herbal agents recited in claim 10 were actually tested in the instant Examples, and page 6, lines 14-20 of the instant specification merely states that they are amyloid inhibitory ingredients. Accordingly, it appears that they are admittedly well known in the art to function as such.

It would have been obvious to employ a therapeutically effective amount of epicatechin, as well as green tea extract - such as beneficially taught by Mitsui Norin and Takami et al., for administering to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to the deposition of beta-amyloid protein on brain nerve cells based upon the beneficial teachings provided therein. [As noted above and in previous Office actions, the reference methods would intrinsically provide the functional effects instant claimed - i.e., would intrinsically treat, inhibit, or manage amyloid fibril formation, deposition, accumulation, aggregation, and/or persistence in a subject suffering from Alzheimer's disease upon such oral

consumption.] It would also have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine green tea extract with one or more of the herbal ingredients recited in claim 10 for the following reasons. It is well known that it is *prima facie* obvious to combine two or more ingredients each of which is beneficially taught and/or admittedly well known by the prior art to be useful for the same purpose (e.g., treating Alzheimer's disease) in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. In re Sussman, 1943 C.D. 518; In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

With respect to the instantly claimed method of using a product-by-process (e.g., clm 31). Please note that in product-by-process claims (including methods of using a product-by-process), "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 and/or 103 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113.

Applicants' arguments have been carefully considered but are not deemed to be persuasive of error in the above art rejections. Applicants argue that the Examiner is implying that beta-amyloid nerve toxicity, or reduction of active oxygen, necessarily (that is, 'inherently') teaches an effect on the treatment of beta-amyloid plaque formation; and also that Dr. Snow says in his Declaration (of August 2003) that at least one study (by Wang) reports that although beta-amyloid mediated neurotoxicity is a focus of intense interest, the underlying mechanisms are still controversial and, further, that no necessary inferences may be drawn from any study of beta-amyloid mediated neurotoxicity. However, the claimed (underlying) functional effect is still deemed to be inherent upon administration of the prior art green tea extracts to a subject suffering from Alzheimer's disease - in which beta-amyloid fibril formations, depositions, aggregations, and/or persistence would inherently be present. Otherwise, the instant invention would not work as claimed/disclosed since beta-amyloid fibril formations, deposits, accumulations, aggregations, and/or persistence would inherently be present in a subject suffering from Alzheimer's disease. [It should be noted that as readily admitted by Applicants, "Alzheimer's disease is characterized by the accumulation of ... beta-amyloid protein or A*B*, in a fibrillar form, existing as extracellular amyloid plaques and as amyloid with the wall of cerebral blood vessels. Fibrillar A*B* amyloid deposition in Alzheimer's disease is believed to be detrimental to the patient and eventually leads to toxicity and neuronal cell death, characteristic hallmarks of Alzheimer's disease. Accumulating evidence implicates amyloid as a major causative factor of Alzheimer's disease pathogenesis" - see page 1, lines 12-18 of the instant specification.] In other words, Applicants appear to be arguing patentability based upon discovering (and claiming) an underlying functional effect concerning how green tea extract

works with respect to treating a subject suffering from Alzheimer's disease. However, as discussed above, this underlying functional effect (i.e., treating/disrupting amyloid fibril formation, deposition, aggregation, and/or persistence) would intrinsically occur in an Alzheimer's patient being administered such a green tea extract - including those disclosed by the cited prior art references.

Applicants further argue that the Examiner is reading into the Mitsui Norin reference something more than it actually contains when he states that it teaches giving green tea "to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to deposition of beta-amyloid protein on brain nerve cells" so that the toxicity of beta-amyloid protein is reduced and, in fact, Mitsui Norin makes no reference whatever to any of these processes. However, the Examiner stands by his interpretation of the Mitsui Norin teachings. As discussed *supra*, Mitsui Norin teaches (and reasonably discloses) the administration of a therapeutically effective amount of epicatechin (which is a naturally occurring compound extracted from green tea) as well as green tea extract, to a subject suffering from Alzheimer's disease so as to inhibit senile plaque formation due to the deposition of beta-amyloid protein on brain nerve cells and, thus, reduce the toxicity of beta-amyloid protein (in particular, see pages 1-2, paragraphs [0033] - [0034] on page 9 of the English translation).

In response to Applicants statement that, in passing, Applicants traverse what the Examiner characterizes as an admission of prior art on page 5, lines 13-16 of the instant specification in that Applicants do not therein admit that catechins are well known to be present in green tea (paragraph bridging pages 7-8 of the 01 April 2005 response), it should be noted that green tea is notoriously well known and recognized in the herbal art to contain naturally

occurring catechins therein including epicatechin (as evidence - see, e.g., the cited Mitsui Norin reference).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Tate whose telephone number is (571) 272-0970. The examiner can normally be reached on Mon-Thur, 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher R. Tate
Primary Examiner
Art Unit 1654